CALIFORNIA INSTITUTE OF TECHNOLOGY INTER-OFFICE MEMO.

TO Dr. J. F. Catchpool FROM Linus Pauling DATE 26 January 1960

SUBJECT Research on anesthetic agents

Here are some suggestions about investigations to be carried out.

On thinking over the matter, I have decided that it may be that some of the hydrogen-bond-forming anesthetic agents act by first combining with side chains of proteins in the brain, or perhaps even with solute molecules. Diethyl ether is a hydrogen-bond-forming agent, as is also ethanol. A probable group with which diethyl ether would combine is the ammonium ion group--it would form a hydrogen bond with the ammonium ion end of the group. I suggest accordingly that we carry out some experiments on formation of hydrates by alkylammonium salts in the presence of diethyl ether.

I suggest that you search the literature to see what you can find about hydrate formation by substances such as the alkylammonium halogenides, especially the chlorides. For example, does ethyl ammonium chloride form a hydrate, or propyl ammonium chloride, or butyl ammonium chloride? If you find that such a hydrate is formed, you could investigate the nature of the crystal formed in case that diethyl ether is present in the system. Even if you do not find any information about hydrate formation, I suggest that you get some butyl ammonium chloride and crystallize it from water, to see what sort of crystals are obtained, and then try crystallizing it from an aqueous solution containing some diethyl ether.

Hydrogen-bond-forming anesthetics which present a proton could be thoroughly investigated in connection with carboxylic acids. Thus for example, you can check on the hydrates of sodium propionate and sodium butyrate, and then on the crystals that are formed when ethanol or tribromoethanol is present also in the system.

Linus Pauling:jh